

THE COUNCIL FOR TOBACCO RESEARCH - U.S.A., INC.

COMMITTEE:

Dr. Bing
Dr. Cattell
Dr. Jacobson

110 EAST 59TH STREET
NEW YORK, N. Y. 10022

Application For Research Grant

Date: July 17, 1972

1. Name of Investigator(s): (include Title and Degrees)

Kurt Amplatz, M. D., Professor of Radiology

2. Institution

Richard Morre, Ph. D., D. Sc., Associate Professor of Radiology

Address:

University of Minnesota Hospitals
Department of Radiology
Minneapolis, Minnesota 55455

3. Short Title of Project:

The Acute Effects of Smoking on the Coronary Artery System in Human Subjects.

4. Proposed Starting Date: As soon as the project is funded

5. Anticipated Duration of this Specific Study: Three years

Brief Description of Objectives or Specific Aims:

There is considerable controversy over the effects of smoking on the cardiovascular system in humans. While there has been much basic research in dogs, human studies have been primarily related to epidemiological studies and post-mortem examinations (1,2). An association between smoking and increased cardiovascular disease has been demonstrated. However, casual relationships have not been defined. Experiments in human subjects relating smoking to acute effects have primarily been electrocardiographic studies and apex cardiograms (3). These studies have indicated a relative myocardial ischemia with increased end diastolic filling pressure of the left ventricle and increased incidence of anginal attacks. The hypothesis is that there is a relative myocardial ischemia secondary to the increased work load of the heart caused by the effects of nicotine. Results from animal experiments confirm the hypothesis. It is our purpose to confirm or refute this hypothesis by performing coronary angiography, left ventriculography, and diastolic pressures, and Xenon 133 myocardial perfusion studies on patients before and after smoking. Only human subjects who are smokers will be used in this study because the effect of nicotine in these subjects might be different from the effect on animals which are obviously nonsmokers.

7. Give a Brief Statement of your Working Hypothesis: Nicotine has been shown in dogs to produce increased coronary blood flow, increased myocardial work load, and increased myocardial oxygen consumption (4,5). It has been hypothesized that this holds true for the human smoker also, but this hypothesis has never been substantiated. Using the tools of coronary angiography, left ventriculography, and diastolic pressures, and Xenon 133 perfusion studies, we hope to be able to prove or to disprove this hypothesis.

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2. Details of Experimental Design and Procedures: (Attach Separate Pages)

Patients with suspected coronary artery disease who are smokers will undergo selective coronary arteriography, and the coronary arteries will be visualized radiographically in at least three projections. The exact diameter of the coronary arteries and areas of narrowing will be measured on the films and expressed in millimeters and percentage narrowing. The patient will be allowed to smoke a cigarette of his choice, a repeat coronary arteriogram will be performed in the identical lateral projection, and the diameter of the coronary arteries and areas of stenoses will again be measured and compared with the presmoking study. By this comparison, we hope to clarify the question whether smoking is a dilator or vasoconstrictor of the coronary arteries. In addition, the transit time of the contrast medium through the vascular bed will be compared. Any change of transit time will strongly suggest a change in capillary resistance due either to vasodilatation or to vasoconstriction.

In another group of patients, end diastolic pressures of the left ventricle will be recorded before and after smoking a cigarette in order to detect any changes in left ventricular function.

The most significant physiologic evaluation will be carried out in another group of patients for whom myocardial tissue blood flow will be measured using the Xenon 133 washout technique. Radioactive Xenon dissolved in saline will be injected selectively into the left coronary artery before and after smoking. Distribution of the isotope and its regional (see attached sheet)

9. Physical Facilities Available (Where Other than Administering Organization Indicate Geographical Location)

Basic Equipment: 1200 MA three-phase generator with rapid roll film see-through changer and 35 mm. cine recording. Physiologic recording equipment for pressures and dye dilution studies. Power injector, defibrillator, automatic processors, etc. Other catheterization laboratories are equipped with biplane film changers.

10. Additional Requirements:

1. A gamma camera with dedicated computer will be mandatory to perform the most important part of this study.

11. Biographical sketches of all principal and professional personnel (append)

12. List of publications: (Five most recent as pertinent) (append)

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3.

13. Budget (1st year)

A. Salaries (Personnel by names)

% time

Amount

Professional

Kurt Amplatz, M. D., Professor of Radiology
 Research Fellow, to be appointed
 Richard Moore, Ph. D., Program Analyst

20%
 100%
 50%

Technical

X-Ray Technician
 Isotope Technician
 Secretary

50%
 50%
 20%

Sub-Total

B. Consumable Supplies (list by categories)

Drugs, contrast media, isotopes, computer
 paper, catheters, guidewires, x-ray film,
 sterile supplies, etc.

Sub-Total

\$ 4,000

C. Other Expenses (itemize)

Travel

1,000

Sub-Total

\$ 1,000

D. Permanent Equipment (itemize)

E. Overhead (15% of A+B+C)

\$ 6,711

Total

\$ 51,449

Estimated Future Requirements:

	Salaries	Consumable Suppl.	Other Expenses	Permanent Equip.	Overhead	Total
Year 2		4,000	1,000		7,065	54,165
Year 3	REDACTED	4,000	1,000		7,440	57,040

It is understood that the applicant and institutional officers
 in applying for a grant have read and found acceptable
 the Council's "Statement of Policy Containing Conditions
 and Terms Under Which Project Grants Are Made."

Signature

Director of Project

Signature

Business Officer of the Institution

Telephone

Telephone

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Continuation of #8

washout will be recorded by a gamma camera, and washout curves will be analyzed by a dedicated computer. Data will be collected, tabulated, and submitted for statistical analysis. From the results, it is hoped to clarify the controversial question of the anatomic and hemodynamic effects of smoking on the human heart. There should not be any significant added hazard. The patient will sign a consent form. The project is presently being considered by the human experimentation committee. The study will be performed in the laboratories of the University of Minnesota Hospitals.

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Other Sources of Financial Support

List financial support for research from all sources, including own institution, for this and/or related research projects.

Current

Title of Project	Source	Amount	Duration
Coronary Revascularization Using an Anger Camera	National Institute of Health	\$ 165,103.00	3 years
Clinical Training in Cardiovascular Radiology	National Institute of Health	\$ 524,938.00	4 years

Pending

Coronary Revascularization Using an Anger Camera (request for supplemental films)

National Institute of Health	\$ 67,310.00
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SECTION II - PRIVILEGED COMMUNICATION

BIOGRAPHICAL SKETCH
 (Give the following information for all professional personnel listed on page 3, beginning with the Principal Investigator. Use continuation pages and follow the same general format for each person.)

NAME Amplatz, Kurt	TITLE Professor of Radiology	BIRTHDATE (Mo., Day, Yr.) R
PLACE OF BIRTH (City, State, Country) R	PRESENT NATIONALITY (If non-U.S. citizen, indicate kind of visa and expiration date) R	SEX <input checked="" type="checkbox"/> Male <input type="checkbox"/> Female

EDUCATION (Begin with baccalaureate training and include postdoctoral)

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	SCIENTIFIC FIELD
Gymnasium, Innsbruck, Austria University of Innsbruck	M. D.		Medicine

HONORS
 Summa cum laude, University of Innsbruck, Austria

MAJOR RESEARCH INTEREST Angiocardiography	ROLE IN PROPOSED PROJECT Project Director
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RESEARCH SUPPORT (See instructions)
 "Clinical Training in Cardiovascular Radiology", PHS 2 T01 HL 5853-04A1, July 1, 1972 - June 30, 1976. \$124,382.00 for four year period.
 "Coronary Revascularization Using an Anger Camera", PHS 1 R01 HE 13998-01, June 1, 1971 - August 31, 1972. \$71,185 for first 15 months. Recommended support for next two years, \$53,679 and \$40,239.

RESEARCH AND/OR PROFESSIONAL EXPERIENCE (Starting with present position, list training and experience relevant to area of project. List all or most representative publications. Do not exceed 3 pages for each individual.)
 Professor, University of Minnesota, 1970
 Associate Professor, University of Minnesota, 1963
 Assistant Professor, University of Minnesota, 1961
 Instructor, University of Minnesota, 1957
 Received medical training in Europe at the Universities of Friburg, Switzerland; Zurich, Switzerland; Paris, France; and Innsbruck, Austria
 Residence training in diagnostic radiology, therapy, and nuclear medicine at Wayne State University, Detroit, Michigan.

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 Rev. 3-70

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SECTION II - PRIVILEGED COMMUNICATION

BIOGRAPHICAL SKETCH

(Give the following information for all professional personnel listed on page 3, beginning with the Principal Investigator. Use continuation pages and follow the same general format for each person.)

NAME Richard Moore	TITLE Associate Professor	BIRTHDATE (Mo., D.) R
PLACE OF BIRTH (City, State, Country) Los Angeles, California, USA	PRESENT NATIONALITY (If non-U.S. citizen, indicate kind of visa and expiration date) U.S. Citizen	SEX <input checked="" type="checkbox"/> Male <input type="checkbox"/> Female
EDUCATION (Begin with baccalaureate training and include postdoctoral)		
INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED
University of Missouri, Columbia, Mo.	B.S.	
University of Rochester, New York	Ph.D.	
George Washington University, Wash. D.C.	D.Sc.	
		SCIENTIFIC FIELD
		Electrical Engineering
		Biophysics
		Biomedical Engineering

HONORS Member:

REDACTED

REDACTED

MAJOR RESEARCH INTEREST Analysis of Physiological Data	ROLE IN PROPOSED PROJECT Biostatistician and Programmer-Analyst
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Special Qualifications:

Dr. Moore is an Associate Professor of Biometry and a member of the American Statistical Society. He is familiar with the application of statistical methods to experimental data. He is certified by the Processing Management Association. He has fifteen years' experience with computers, and he is an Associate Professor of Health Computer Sciences. He has over sixty publications in these fields.

RESEARCH AND/OR PROFESSIONAL EXPERIENCE (Starting with present position, list training and experience relevant to area of project. List all or most representative publications. Do not exceed 2 pages for each individual.)

PROFESSIONAL EXPERIENCE:

- 1969 - Present:
University of Minnesota, Department of Laboratory Medicine.
Associate Professor (Joint Appointments in Biometry, Radiology, and Biophysics).
- 1960 - 1969:
American National Red Cross, Washington, D.C. and Bethesda, Maryland
Chief, Biophysics Section, Blood Research Laboratory.
- 1968 - 1969:
George Washington University, Washington D.C.
Visiting Professor (Radiation Biology), Department of Radiology.
- 1965 - 1968:
George Washington University, Washington, D.C.
Visiting Assistant Professor, Department of Physiology.
- 1957 - 1960:
National Institutes of Arthritis & Metabolic Diseases
Scientist
- 1955 - 1957:
Public Health Service
Commissioned Officer Radiological Health Program.

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12. List of publications: (Five most recent as pertinent).

Kurt Amplatz, M. D.

1. White, R. I., Jr.; Frech, R. S.; Castaneda, A.; and Amplatz, K.: The Nature and Significance of Anomalous Coronary Arteries in Tetralogy of Fallot. Am. J. Roentgenol. Radium Ther. Nucl. Med. 114: 2, pp 350-354, February, 1972.
2. White, R. I., Jr.; Frech, R. S.; and Amplatz, K.: An Improved Technique for Right Coronary Artery Catheterization. Am. J. Roentgenol. Radium Ther. Nucl. Med. 113: 3, pp 562-566, November, 1971.
3. Chapter "The Value of Vectorcardiography, Electrocardiography and Exercise Electrocardiography in the Diagnosis of Coronary Artery Disease. Correlation with Coronary Arteriography." in VECTORCARDIOGRAPHY 2. Naip Tuma, M. D.; Gerald B. Lee, M. D.; and Kurt Amplatz, M. D. Proceedings of the XI International Symposium on Vectorcardiography. North-Holland Publishing Company. Editor I. Hoffman, Co-editors R. I. Hamby and E. Glassman, 1971.
4. Snyder, C.; Cramer, R.; and Amplatz, K.: Isolation of Sodium as a Cause of Ventricular Fibrillation. Invest. Radiol. 6:245-248, July-August, 1971.
5. Loken, M. K.; White, R. I., Jr.; Ponto, R. A.; Frech, R. S.; and Amplatz, K.: Intravenous Radioisotope Angiography with Computer Processing of Data. (abstract). J. Nucl. Med. 12: 448, June, 1971.

Richard Moore, Ph. D.

1. Moore, R.; Ledley, R. S.; and Sing, H. C.: Application of Automatic Processing Methods to the Radiologic Image. The radiologic Clinics of North America, 7: 473-483, December, 1969.
2. Moore, R. and Wingert, R. A.: Calibration of Laboratory Instruments by Computer. Medical Electronics and Data, 1: 76-82, April, 1970.
3. Moore, R. and Ledley, R. S.: Evaluation of the Significance of Coherent Scattering of an X-Ray Beam to Darkening of Radiographic Film. (In) Proceedings of Bone Measurement Conference. (Ed.) J. R. Cameron, Atomic Energy Commission, CONF-700515, pp. 205-233, 1970.
4. Moore, R.; Ledley, R. S.; and Sing, H. C.: Application of Automatic Processing Methods to Radiologic Images. Yearbook of Radiology, 10-11, 1971.
5. Moore, R.: Computer Calculation of Ventricular Volume From Roentgenograms. Medical Electronics and Data, 2: 56-61, 1971.

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REFERENCES

1. Auerbach, O., et al.: Thickness of Walls of Myocardial Arterioles in Relation to Smoking and Age. Arch. Environ. Health 22:20-27, January, 1971.
2. Seltzer, C. C.: The Effect of Cigarette Smoking on Coronary Artery Disease. Arch. Environ. Health 20: 418, March, 1970.
3. Aronow, W. S.: The Effect of Smoking Cigarettes on the Apexcardiogram in Coronary Heart Disease. Chest 59: 365-368, April, 1971.
4. Ross, G. and Blesa, M. I.: The Effect of Nicotine on the Coronary Circulation of Dogs. Amer. Heart J. 79: 96-102, January, 1970.
5. Leb, G., et al.: The Effect of Nicotine on Effective and Total Coronary Blood Flow in the Anesthetized Closed-Chest Dog. J. Pharmacol. Exp. Ther. 173: 138, May, 1970.

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